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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,090	02/03/2004	Margaret H. Baron	HC-P02-060	4153
28120	7590	01/03/2012	EXAMINER	
ROPE & GRAY LLP IPRM - Floor 43 PRUDENTIAL TOWER 800 BOYLSTON STREET BOSTON, MA 02199-3600			HOWARD, ZACHARY C	
			ART UNIT	PAPER NUMBER
			1646	
			NOTIFICATION DATE	DELIVERY MODE
			01/03/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPatentMail@ropesgray.com
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Office Action Summary	Application No. 10/772,090	Applicant(s) BARON ET AL.	
	Examiner ZACHARY HOWARD	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 November 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 70-75 is/are pending in the application.
- 5a) Of the above claim(s) 73 and 74 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 70-72 and 75 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☒ Claim(s) 70-75 are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 03 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/16/11</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Status of Application, Amendments and/or Claims

A new listing of the claims was filed on 11/16/11. No amendments to the claims have been made. The new listing is entered in full.

Claims 70-75 are pending in the instant application.

Claims 73 and 74 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 70-72 and 75 are under consideration, as they read upon the elected species.

Maintained Objections and/or Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 70-72 and 75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection was set forth previously and maintained at pg 2-13 of the 7/19/11 Office Action.

Applicants' arguments (11/16/11, pg 3-5) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In section A of the 11/16/11 response (pg 3-4), Applicants repeat arguments advanced previously in section A of the 3/24/10 response (pg 3-4), including pointing to MPEP 2164.02 and the previously submitted references of Valone et al (1995; Exhibit A) and Weiner et al (1995; Exhibit B).

These arguments have been fully considered but are not found to be persuasive. These arguments were addressed previously at page 8-9 of the 7/19/11 Office Action, and this response is maintained herein.

In section B of the response (pg 4-5), Applicants argue that as discussed in *In re Wands*, a claimed invention need not be associated with complete success in order to be considered enabled by an application, and "partial success" may be considered sufficient for demonstrating enablement. Applicants argue that the skilled worker would have considered at the earliest effective filing date of the application that a given treatment or therapy for cancer would be enabling if even a small percentage of a patient population had tumor regression induced and would not have expected it to cure each and every cancer patient. Applicants argue that the state of art for cancer therapies is administration for general rather than personal cancer treatment. In support of this argument Applicants point to teachings concerning the cancer treatment docetaxel; specifically Sulkes et al (1994; Exhibit C) and Brown et al (2004; Exhibit D). Applicants argue that docetaxel has become a successful cancer treatment despite only being shown capable of inducing partial remission in a relatively small subset of treated patients during Phase II clinical trials as taught by Sulkes et al. Applicants argue that docetaxel resistance in breast cancer cells is associated with reduced p27 expression (per Brown et al) but there is no evidence that breast cancer patients are screened for p27 expression prior to docetaxel treatment. Applicants further argue that the claimed method is effective in treating a number of different tumor types; in support Applicants point to Bailey et al (1999; Exhibit E); Yauch et al, 2008 (Exhibit F); Coon et al (2010; Exhibit G) and Berman et al (2003; Exhibit H). Applicants argue that the skilled artisan would not have been required to perform any undue experimentation to use the claimed method in view of the wide variety of tumor types in which the claimed method has been shown to be effective, combined with the skilled worker's expectation that a given cancer therapy would be ineffective in at least a subset of tumors.

These arguments have been fully considered but are not found to be persuasive. As set forth in the rejection of record, the instant specification contains *de minimis* guidance regarding the ability of a Sonic hedgehog blocking antibody to treat solid

Art Unit: 1646

tumors; the specification merely asserts that such can be used to treat all forms of solid tumors without any evidence in support of such. There is no "partial" success demonstrated in the instant application. The teachings in the art submitted by Applicants regarding docetaxol are clearly different from the teachings of the instant application. Sulkes et al (1994; Exhibit C), prior to conducting the clinical trial referenced by Applicants, teach that "[i]t has demonstrated activity against a variety of preclinical tumor models" (pg 389). This teaching demonstrates the type of guidance missing from the instant application, and shows the standard of experimentation in the art prior to practicing a method of treatment of tumors. Brown et al (2004; Exhibit D) was published ten years after Sulkes et al and thus also builds on the guidance of previous studies. In contrast, based on the minimal teachings in the instant specification, the skilled artisan at the claimed priority date would not have predicted that "cancer" or even the elected species of "breast cancer" could be treated with a Sonic hedgehog blocking antibody without further experimentation to determine if such was possible. Furthermore, the rejection of record set forth that the post-filing date art makes it clear that many solid tumors do not include dysfunctions that lead to Shh overexpression, citing Thievensen et al (2005), Watkins et al (2003), Chatel et al (2007); Thomas et al (2011), U.S. Pre-Grant Application Publication 2004/0110663. The instant specification only suggests treatment of "solid tumors" generally and "breast cancer" specifically, with no guidance regarding specific types of cancer that may have hedgehog overexpression. The new references cited by Applicants do not contradict the teachings of the references of record. In Bailey et al (2009; Exhibit E) and Coon et al (2010; Exhibit G) the experimentation is limited to use of a cancer sample (pancreatic or medulloblastoma, respectively) already known to be overexpressing Shh. Yauch et al (2008; Exhibit F) teach that "subsets of human tumours and cell lines do indeed express Hh ligands. Microarray expression analysis of human tissue specimens revealed that subsets of colorectal, endometrial, ovarian and pancreatic cancers overexpressed Hh ligand mRNA" (pg 406). Berman et al (2003; Exhibit H) found that the Hh pathway is not active in colon tumor derived cell lines (pg 847). Thus, it is maintained that the post-filing date art makes it clear that many solid tumors do not include dysfunctions that lead to Shh

Art Unit: 1646

overexpression, and that the skilled artisan would predict that a breast cancer tumor that does not overexpress the Sonic hedgehog protein would fail to be inhibited by administration of a Sonic hedgehog blocking antibody. It is maintained that in view of the lack of guidance provided by the specification and the prior art the skilled artisan could not practice the claimed method without undue experimentation.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Bridget E Bunner/
Primary Examiner, Art Unit 1647